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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/534,257	05/10/2005	Shoji Furusako	1110-0326PUS1	4508

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EXAMINER	
WEN, SHARON X	

ART UNIT	PAPER NUMBER
1644	

NOTIFICATION DATE	DELIVERY MODE
02/28/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/534,257	FURUSAKO ET AL.	
	Examiner	Art Unit	
	SHARON WEN	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The examiner of this application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Sharon Wen, Group Art Unit **1644**, Technology Center 1600.

2. Applicant's amendment, filed 11/28/2007, has been entered.

Claims 1-22 have been canceled.

Claims 23-26 have been added and are currently pending.

Election/Restrictions

3. Applicant's election without traverse of Group II in Response to Election / Restriction, filed 11/28/2007, is acknowledged. Because of the cancellation of claims 1-22, the restriction requirement, mailed 09/28/2007, is rendered moot.

Claims 23-26 are currently under examination as they read on the elected invention of an assay method or a diagnostic method for human low-molecular-weight CD14.

Priority

4. The domestic priority date for claims 23-26 is deemed the effective filing date of PCT/JP03/14389, i.e., 11/12/2003.

5. Applicant's claim for foreign priority is acknowledged. However, as there does not appear to be certified English translation of Japanese priority applications, 2002-328866 and 2003-330775, Examiner thus cannot determine whether the priority applications provide sufficient written support for the present claims under examination.

Information Disclosure Statement

6. Applicant's IDS's, filed 01/28/2008, 05/18/2007, 05/18/2007, 04/06/2007, 09/13/2006, 08/11/2006, 08/16/2005, 07/01/2005, 05/10/2005, are acknowledged, and have been considered.

Specification

7. Applicant is requested to review the application for spelling error, the use of trademarks, embedded hyperlinks and/or other form of browser-executable code.

Trademarks should be capitalized wherever it appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Embedded hyperlinks and/or other form of browser-executable code are impermissible in the text of the application as they represent an improper incorporation by reference.

Claim Rejections - 35 USC § 112 second paragraph

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 23-26 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The present claims are incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01.

The present claims are drawn to a method of detecting CD14 using two antibodies in a sandwich immunoassay. However, the claims do not recite sufficient method steps that define the metes and bounds of the claims, e.g., contacting step, detecting step, measuring step and resolution step.

Applicant is reminded that any amendment MUST point to a basis in the specification so as not to add New Matter. See MPEP 714.02 and 2163.06.

Claim Rejections - 35 USC § 112 first paragraph

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 23-26 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

A) *The following grounds of enablement rejection pertain to diagnosing sepsis:*

Claims 25-26 are directed to a method of diagnosing sepsis comprising measuring an amount of human low-molecular weight CD14. Although claims 23-24 do not recite "diagnosing sepsis", given that the only disclosed utility for the method of detecting human low-molecular weight CD14 is for diagnosing sepsis, claims 23-24 also read on the method of diagnosing sepsis and thus are included in the rejection herein.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention, see *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

With regards to the instant claims, their breadth, the state of the prior art, and the lack of guidance provided by the inventor, comprise the primary issues as regards the unpredictability of the claimed method.

The instant claims are directed to a method of diagnosing sepsis comprising measuring human low-molecular weight CD14. However, the specification does not enable one of skill in the art, at the time the invention was made, to practice the claimed methods.

A medical diagnosis is a process of identifying a medical condition or disease by its signs, symptoms, and from the results of various diagnostic procedures. A person of skill in the art, at the time of the invention was made, was well-aware that sepsis is difficult to diagnosing. For example, according to Levenson (*Clinical Laboratory News* 2008, Volume 34, Number 1, [retrieved on 02/12/2008]. Retrieved from the Internet: < URL: http://www.aacc.org/AACC/publications/cln/2008/jan/cover1_0108.htm>, page s1-8), there is not individual marker that can be used for diagnosing sepsis with 100% certainty (see page 2).

Furthermore, simple correlation of elevated level of low-molecular weight CD14 does not amount to diagnosis of any particular disease because, according to the state of the art, elevated levels of low-molecular weight CD14 are associated with numerous diseases other than sepsis. For example, low-molecular weight CD14 level is higher in patients with malaria (Weinisch et al. *Clin Exp Immunol* 1996, 105:74-78, see entire document); and low-molecular weight CD14 level is higher in patients with HIV and rheumatoid arthritis (Lien et al. *Blood* 1988, 92:2084-2092, see Introduction).

Similarly, there is insufficient guidance and instruction provided by Applicant, at the time of filing, as to how to correlate elevated low-molecular weight CD14 level to any specific disease such as sepsis encompassed by the instant claims.

Several variables are used in evaluating the predictability of detection or diagnostic assays. These include diagnostic specificity and sensitivity and positive and negative predictive values.

The sensitivity of an assay reflects the fraction of those subjects with a specific disease that the assay correctly identifies as positive; while the specificity of an assay reflects the fraction of those subjects without the disease that the assay correctly identifies as negative.

The positive predictive value refers to the probability that an individual with a positive test result has the diseases; while the negative predictive value refers to the probability that an individual with a negative test result does not have the disease.

There is an inverse relationship between the sensitivity and specificity, which is related to the assigned cutoff value that is used for a particular test to segregate diseased populations from those with no disease.

In the absence of objective evidence to the contrary and keeping with the nature of evaluating a number of potential blood enzyme for diagnosis, the skilled artisan would predict that there is an overlap between diseased and non-diseased groups, i.e. individuals without a disease may exhibit abnormal levels of low-molecular weight CD14, while individuals with the disease may also exhibit normal levels of low-molecular weight CD14.

Here, Applicant has not provided sufficient direction and guidance as to the sensitivity and specificity of detecting sepsis via the use of CD14-specific antibodies alone.

Additionally, applicant has not set forth normal values as well as those values that would lead the skilled artisan to predict the ability to detect a disorder involving elevated levels of low-molecular weight CD14 in serum or plasma.

The cutoff value for a particular assay will determine the diagnostic sensitivity and specificity of the test based on the number of individuals that are diagnosed with and without the disease.

There is insufficient objective evidence that the claimed assay which relies upon the detection of low-molecular weight CD14 in serum or plasma samples obtained from various patients provides the requisite sensitivity and specificity to be useful for the claimed purpose detecting a sepsis via the use of CD14-specific antibodies alone.

Given the unpredictability of the art in diagnosing sepsis and correlation of low-molecular weight CD14 with any disease, and lack of guidance and working examples in the present application, the experimentation left to those skilled in the art, would be unnecessarily, and improperly, extensive and undue.

In view of the lack of predictability of the art to which the invention pertains the lack of established clinical protocols for effective methods to diagnose atherosclerosis, undue experimentation would be required to practice the claimed methods of diagnosing atherosclerosis with a reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to effectively practice the claimed methods and absent working examples providing evidence which is reasonably predictive that the claimed methods are effective for diagnosing the diseases or disorders encompassed by the claimed methods.

B) *The following grounds of enablement rejection pertain to a biological deposit:*

It is apparent that F1025-3-1 antibody is required to practice the claimed invention. As required elements, they must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If they are not so obtainable or available, the enablement requirements of 35 USC 112, first paragraph, may be satisfied by a deposit of the monoclonal antibodies. See 37 CFR 1.801-1.809.

In addition to the conditions under the Budapest Treaty, Applicant is **required** to satisfy that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent in U.S. patent applications.

Amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If the original deposit is made after the effective filing date of an application for patent, the applicant should promptly submit a verified statement from a person in a position to corroborate the fact, and should state, that the biological material which is deposited is a biological material specifically identified in the application as filed, except if the person is an attorney or agent registered to practice before the Office, in which the case the statement need not be verified. See MPEP 1.804(b).

Conclusion

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHARON WEN whose telephone number is (571)270-3064. The examiner can normally be reached on Monday-Thursday, 8:30AM-6:00PM, ALT. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara can be reached on (571)272-0878. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sharon Wen, Ph.D./
Examiner, Art Unit 1644
February 13, 2008

PHILLIP GAMBEL, PH. D.
PRIMARY EXAMINER
TC1600
2/13/08